REMARKS

Applicants wish to thank the Examiner for acceptance of the Request for Continued Examination, and for reviewing the pending claims. By this amendment, claims 55, 56, and 62 are canceled. Further, new claims 67 through 73 have been added by this amendment. Therefore, Claims 40 through 54, 57-61, and 63-73 are now pending. No new matter has been added by this amendment.

Regarding the Rejections under 35 U.S.C. § 112

The Examiner rejected Claims 55 and 56 under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. Accordingly, please cancel Claims 55 and 56.

The Examiner rejected Claims 40-47 and 49-66 under 35 U.S.C. § 112, first paragraph, alleging that the specification, although enabling for methods of producing an immunogenic composition from *L. fermentum*, does not provide enablement for methods of producing an immunogenic composition from any peptidoglycan containing bacteria. The Examiner further alleges that extrapolation of a working example of *L. fermentum* to any peptidoglycan-containing bacterial species would require excessive experimentation. The Applicants disagree.

Enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive." *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986). "To be enabling, the specification of a patent must teach those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation' ... Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *See In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993).

There is ample support throughout the specification for the use of any peptidoglycan-containing bacteria. Though it is mentioned that the preferred bacterial species is *L. fermentum*,

the specification notes that other species may be used. For example, the presence of peptidoglycan in bacteria containing a cell wall, particularly in Gram positive bacteria, is clearly taught in the specification:

"All bacteria containing a cell wall, and particularly Gram positive bacteria, possess a specific component of the cell wall called peptidoglycan. The peptidoglycan provides structural support to the bacterial cell. A very early finding in the field of microbiology was that there was considerably more peptidoglycan in the Gram positive cell wall then in the Gram negative cell wall of bacteria, causing the differential Gram staining of such bacteria" (page 1, line 29 – page 2, line 3).

The teaching that any gram positive bacteria can be used to prepare an immunostimulatory composition by the method of the invention is clearly demonstrated throughout the specification. For example:

"The general principle of the invention is to generate anti-cancer, immunostimulatory water-soluble extracts of Gram-positive bacteria such as Lactobacillus fermentum using an acid" (page 2, lines 28-30).

The teaching that any peptidoglycan-containing bacteria can be used to prepare an immunostimulatory composition by the method of the invention is clearly demonstrated throughout the specification. For example:

"One embodiment of the invention is a method for producing an immune stimulating composition by treating a bacteria containing peptidoglycan with acid..." (page 3, lines 1-2).

Further, although it is clearly indicated that the preferred genus is *Lactobacillus*, and the preferred species is *L. fermentum*, it is also clear that any bacterial species containing peptidoglycan may be used:

"*The bacteria containing peptidoglycan is preferably Lactobacillus, more preferably L. fermentum*" (page 3, lines 11-12).

Thus, while the use of *L. fermentum* is taught as the "best mode" of the invention, the possibility of using any other bacterial species, as long as it contains peptidoglycan, is also taught.

Further, it would not be difficult for one of skill in the art, after reading the specification, to grow, prepare, and test a bacterial extract made from any peptidoglycan-containing bacterial species. Methods of growing bacterial cultures are known in the art, and are also described in Examples 1 and 2. Methods of preparing and treating the extract are described throughout the specification, while specific examples are detailed in Examples 1 and 2. One of skill in the art, after reading the specification, could follow the method of the instant invention using any desired species of peptidoglycan-containing bacteria.

Assays of immunostimulatory activity can be performed, for example, using the methods described in Example 3 (page 6, line 1 through page 8, line 3). This example clearly shows how to test an extract from any bacterial species for its immunostimulatory effects after preparation by the method of the invention. Methods of examining lymphocyte proliferation are shown on page 6, lines 21 through 31 and Figure 1. Methods of analyzing cytokine production are shown on page 7, lines 1-18. Further, methods of examining dendritic cell maturation are shown on page 7, line 19 through page 8, line 3. Thus, one of skill in the art, after reading the instant specification, would be able to test any peptidoglycan-containing bacterial organism for immunostimulatory activity after preparation by the method of the invention.

In summary, the claimed invention is described in sufficient detail to demonstrate that the inventors had possession of the claimed invention. For all of the above reasons, Applicants respectfully request withdrawal of all rejections under 35 U.S.C. § 112, and allowance of the pending application.

Discussion of Rejection Under 35 U.S.C. § 102 and 103

The Examiner has rejected Claims 40-42, 45-50, 58-61, and 63-65 under 35 U.S.C. § 102(b) as being anticipated by, or, in the alternative, under 35 U.S.C. § 103(a) as being obvious over Link (U.S. Patent Number 5,185,321).

Regarding the Rejection Under 35 U.S.C. § 102(b)

The Applicants assert that the claimed invention is novel in view of the Link reference. To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. ...There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991).

The prior art cited by the Examiner does not teach or suggest the claimed invention. Link discloses a method of preparing immunostimulating compounds (for oral administration) by adding the enzyme lysozyme to a bacterial mixture (*Lactobacillus bulgaris* alone or *Lactobacillus bulgaris* plus *Streptococcus thermophilus*). The bacterial mixture, once digested with lysozyme, produces a composition "rich in N-acetyl muramyl peptides." The Link reference contains no teaching or suggestion that the immunostimulatory products can prepared without the presence of lysozyme. Indeed, the presence of lysozyme is essential to Link's method.

The present invention, in contrast, is directed to a different immunostimulating composition, which is prepared by treating a bacterial mixture with an acid treatment solution. These two methods of preparing the compositions lead to different types of resultant fragment molecules. An example of the difference between the acid or acid/heat treatment and an enzyme treatment can be seen in table 3, (page 10, line 11) of the instant specification, where it is shown

that cell wall enzymes create completely different fragment compositions than the acid treatment of the invention.

Considering the above, it is clear that Link teaches a different method to produce a product having a different composition. Therefore, Link does not teach or suggest the claimed invention.

Further, the compositions of the present invention are in a form that is suitable for administration by injection. In contrast, the Link reference teaches only oral administration of its composition. The Link reference contains no suggestion to inject its composition, nor any suggestion to administer by any means other than orally. In fact, if one were to inject a composition which contains large amounts of lysozyme into the blood stream, results would be likely to be deleterious (or even toxic). Thus, the Link reference teaches away from the claimed invention, because it describes a composition that, if administered in the form intended by the present invention, would produce a seemingly nonfunctional, even harmful, product (*See* In re Sponnable, 405 F.2d 578, 587, 160 USPQ 237, 244 (CCPA 1969) (holding that cited references taught away because the combination of reference "would produce a seemingly inoperative device").

For all of the above reasons, Applicants respectfully request withdrawal of all rejections under 35 U.S.C. § 102, and allowance of the pending application.

Regarding the Rejection Under 35 U.S.C. § 103(a)

The Examiner also rejected Claims 40-42, 45-50, 58-61, and 63-65 under 35 U.S.C. § 103(a) as being unpatentable over Link (U.S. Patent Number 5,185,321). To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

The Link reference does not teach all of the limitations of the claimed invention. Specifically, claims previously receiving a 102/103 rejection based on Link have now been amended to depend from new claim 67, which contains a limitation that the acid treatment step occurs at a final pH of about 2.0. The Link reference does not teach the use of an acid treatment at a final pH of about 2.0. Accordingly, the third requirement of the three-pronged test for obviousness is not met, and thus the claims, as now amended, are nonobvious in view of the cited prior art.

For all of the above reasons, Applicants respectfully request withdrawal of all rejections under 35 U.S.C. § 103, and allowance of the pending application.

CONCLUSION

Applicants have attempted to address each of the issues raised in the Office action. Applicants respectfully submit that the application is now in condition for allowance, which action is earnestly solicited. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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By: Suzanne Jepson

Suzanne G. Jepson, Ph.D.
Registration No. 51,848
Agent of Record
Customer No. 20,995
(619) 235-8550